510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k130276

B. Purpose for Submission:

Change to an existing device - Change in the photomultiplier tube (PMT) for Dimension EXL with LM system (previously cleared in k073604)

C. Measurand:

Free Thyroxine

D. Type of Test:

Quantitative, automated chemiluminescent immunoassay

E. Applicant:

Siemens Healthcare Diagnostics

F. Proprietary and Established Names:

Dimension FT4L Flex reagent cartridge

Dimension® EXL™ with LM System

G. Regulatory Information:

1. Regulation section:

   21 CFR §862.1695, Free Thyroxine

   21 CFR §862.2160, Discrete photometric chemistry analyzer for clinical use

2. Classification:

   Class II, Class I

3. Product code:

   CEC, JJE

4. Panel:

   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below

2. Indication(s) for use:
   The Dimension® EXL™ with LM system is an in vitro diagnostic device that is intended to measure a variety of analytes in human body fluids. The system utilizes photometric, turbidimetric, chemiluminescence and integrated ion selective multisensory technology for chemical and immunochemical applications for clinical use.

   The FT4L method is an in vitro diagnostic test for the quantitative measurement of Free Thyroxine in human serum and plasma on the Dimension EXL™ with LM system. Measurements of free thyroxine are used in the diagnosis and monitoring of thyroid disease.

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   Dimension® EXL™ with LM System

I. Device Description:

The Dimension EXL with LM system is a floor model, fully automated, microprocessor-controlled, integrated instrument which used prepackaged Siemens Dimension Flex reagent cartridges to measure a variety of analytes in human body fluids. The system can process samples in random access, batch or STAT modes. The instrument has a heterogeneous module (HM) for processing chromium-based heterogeneous immunoassays and a LOCI module (LM) for chemiluminescent immunoassays.

The test system remains the same except for the PMT. The PMT was modified by changing the supplier and the format of the multiplier channel was changed from multiple dynodes to enhanced glass single surface tube used to count the signal for the chemiluminescent methods.

The Dimension® FT4L Flex® regent cartridge consists of prepackaged liquid reagents containing two synthetic beads, and a biotinylated anti-T4 mouse monoclonal antibody in a plastic eight-well cartridge

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Dimension® EXL™ with LM system including FT4L assay

2. Predicate 510(k) number(s):

   k073604

3. Comparison with predicate:

Similarities		
Item	Device: Dimension® EXL™ with LM with new PMT	Predicate: Dimension® EXL™ with LM (k073604)
Intended/ Indications for Use	The Dimension® EXL™ with LM system is an in vitro diagnostic device that is intended to measure a variety of analytes in human body fluids. The system utilizes photometric, Turbidimetric, chemiluminescence and integrated ion selective multisensor technology for chemical and immunochemical applications for clinical use.	Same
System Control	Fully automated and controlled by microprocessors	Same
User Interface	Contains graphical user interface screens	Same
Detection Technologies	Contains a photometer, a heterogeneous module and a multisensor electrode for performing photometric tests, and electrolyte tests. It also has a LOCI module for high sensitivity homogenous immunoassay tests.	Same
Reagents	Uses pre-packaged Flex reagent cartridges. Reagents are hydrated and stored on-board the instrument	Same
Temperature	Reagents are stored at 2-8°C. Reactions are controlled at 37°C.	Same
Operating System	LINUX Operating System	Same

Differences		
Item	Device: Dimension® EXL™ with LM with new PMT	Predicate: Dimension® EXL™ with LM (k073604)
Photomultiplier tube used to amplify the signal in the chemiluminescent methods	Multiplier channel: multiple dynodes	Multiplier channel: Enhanced Glass Single Surface tube

Similarities and Differences for Dimension® FT4L Flex® reagent cartridge

Similarities and Differences		
Item	Device: Dimension® FT4L Flex® reagent cartridge	Predicate: Dimension® FT4L Flex® reagent cartridge (k073604)
Intended Use	The FT4L method is an *in vitro* diagnostic test for the quantitative measurement of Free Thyroxine in human serum and plasma on the Dimension® EXL™ with LM system. Measurements of free thyroxine are used in the diagnosis and monitoring of thyroid disease.	Same
Assay Range	0.1-8.0 ng/dL	Same
Sample Type	Human serum and plasma	Same
Technology	LOCI® technology	Same
Sample size	10 µL	Same
Reagents and antibody	There are three (3) reagents- Streptavidin sensibeads, T3 Chemibeads and FT4 biotinylated antibody (containing mouse monoclonal antibody)	Same

K. Standard/Guidance Document Referenced (if applicable):

- CLSI-EP05-A: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline
- CLSI-EP09-A: Method Comparison and Bias Estimation Using Patient Samples: Approved Guideline
- In Vitro Diagnostic Devices: Guidance for the Preparation of 510(k) Submissions-Jan. 1997
- Format for Traditional and Abbreviated 510(k)'s-Guidance for Industry and Staff-Nov. 17, 2005 Guidance for Industry and FDA staff: Administrative Procedures for CLIA Categorization- May 7, 2008

L. Test Principle:

The Dimension EXL with LM system is a floor model, fully automated, microprocessor controlled, integrated instrument which uses prepackaged Siemens Dimension Flex® reagent

cartridges to measure a variety of analytes in human body fluids. The system can process samples in random access, batch or STAT modes. The instrument has a heterogeneous module (HM) for processing chromium-based heterogeneous immunoassays and a LOCI® module for chemiluminescent immunoassays. The instrument can also perform photometric, turbidimetric and affinity column mediated immunoassay (ACMIA) tests.

The FT4L method is a homogeneous, sequential, chemiluminescent immunoassay based on LOCI® technology. The LOCI® reagents include two synthetic bead reagents and a biotinylated anti-T4 mouse monoclonal antibody. The first bead reagent (Chemibeads) is coated with triiodothyronine (T3), a naturally occurring, weaker binding analog of T4, and contains chemiluminescent dye. The second bead reagent (Sensibeads) is coated with streptavidin and contains a photosensitizer dye. In a first step, sample is incubated with biotinylated antibody which allows T4 from the sample to saturate a fraction of the biotinylated antibody that is directly related to the free thyroxine (FT4) concentration. In a second step, T3 Chemibeads are added and form bead/biotinylated antibody immunocomplexes with the non-saturated fraction of the biotinylated antibody. Sensibeads are then added and bind to the biotin to form bead pair immunocomplexes. Illumination of the complex at 680 nm generates singlet oxygen from Sensibeads which diffuses into the Chemibeads, triggering a chemiluminescent reaction. The resulting signal is measured at 612 nm and is an inverse function of the FT4 concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   The precision study was conducted using three (3) commercial quality controls (BioRad Liquichek Immunoassay QC) and two (2) patient serum pools. Testing was performed over twenty (20) days, one (1) run per day for each test material on the Dimension EXL with LM systems with both the new and the current PMT. Analysis of variance was used to evaluate the data as outlined in CLSI EP5-A2 Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline-Second Edition. The data is summarized below.

Current PMT FT4L assay		Repeatability (within-run)		With-in Lab	
Sample	**Mean (ng/dL)**	**SD (pg/mL)**	**%CV**	**SD (pg/mL)**	**%CV**
Level 1	0.91	0.02	2.5	0.03	3.0
Level 2	2.39	0.06	2.4	0.08	3.0
Level 3	7.01	0.01	2.5	0.03	3.0
Patient Pool 1	1.18	0.03	2.5	0.03	3.0
Patient Pool 2	3.86	0.07	1.7	0.08	2.0

New PMT FT4L assay		Repeatability (within-run)		With-in Lab	
Sample	**Mean (ng/dL)**	**SD (pg/mL)**	**%CV**	**SD (pg/mL)**	**%CV**
Level 1	0.89	0.02	2.0	0.03	3.4
Level 2	2.44	0.05	1.9	0.07	2.8
Level 3	6.85	0.10	1.5	0.17	2.4
Patient Pool 1	1.17	0.02	1.7	0.03	2.7
Patient Pool 2	3.93	0.06	1.6	0.07	1.7

b. Linearity/assay reportable range:

The measuring range was determined using the Level 5 Thyroid Calibrator and the calibrator base matrix with the new PMT in accordance with CLSI Evaluation of Linearity of Quantitative Measure Procedures (EP06-A). Intermediate levels were prepared by proportional mixing of the high and low calibrator materials to produce concentrations evenly distributed across the assay range. Eleven concentration levels (ranging 0.1 to 8.32ng/dL) were assayed three times. The data was analyzed using least squares linear regression. The quadratic terms of the second and third order polynomial fit were statistically insignificant (p value >0.05), supporting linearity across the measuring range of 0.1 to 8.0ng/dL. The least squares linear regression analyses were: slope =1.04, y-intercept= -0.01, and R^2=1.00.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):
Calibrator Traceability:

USP-grade thyroxine is spiked into stripped human serum at different concentrations. This becomes the "Anchor Pool". The "Anchor Pool" values are validated in-house.

A Master Pool is developed from stripped bovine albumin to which different concentrations of thyroxine have been added. Values for the Master Pool are derived by multiple analyses against the Anchor Pool calibration curve. LOCI® Thyroid Calibrator value assignment is established by measurement against the Master Pool calibration.

Calibrators have been previously cleared in k073604.

d. Detection limit:

To verify the limit of blank (LoB), twenty (20) replicates of the calibrator matrix material (0 ng/dL) were processed in a single batch run in accordance with CLSI EP17-A with the new PMT. None of the replicate measurements exceeded the LoB claim of 0.03ng/dL. The LoB claim was verified and established as 0.03ng/dL the reference concentration for LoD verification.

To verify the limit of detection (LoD), two samples were prepared at concentrations approximately equal to the LoD claim (0.06 ng/dL). The samples were processed in

replicates of five for three testing days yielding a total of fifteen test measurements per sample. All replicate measurements exceeded the LoB claim. The LoD was determined to be 0.06 ng/dL.

e. Analytical specificity:

Provided in k073604

f. Assay cut-off:

Provided in k073604

2. Comparison studies:

a. Method comparison with predicate device:
Forty five (45) patient samples across the FT4L assay range were tested on modified and unmodified instruments. The results were analyzed by Passing Bablok and linear regression statistics. The correlation coefficient was obtained by linear regression. The summary of the method comparison data is presented below.

Method	**Range (ng/mL)**	**Slope (95% CI)**	**Intercept ng/dL (95% CI)**	**Correlation Coefficient (std linear regression)**	**n**
FT4L (Passing Bablok)	0.23-7.78	0.99 (0.96- 1.01)	-0.03 (-0.07-0.00)	Not applicable	45
FT4L (linear regression)	0.23-7.78	0.97	0.00	0.998	45

b. Matrix comparison:

Provided in k073604

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off**:**

   Not applicable.

5. Expected values/Reference range:

   The expected values were transferred from that previously determined for the FT4 method on the Dimension Vista System. The values represent the central 95% of results determined non-parametrically from a population of 199 healthy adults (140 males and 59 females).

   The expected values provided in the labeling are: 0.76-1.46 ng/dL.

N. Instrument Name:

Dimension® EXL™ with LOCI Module (LM) System

O. System Descriptions:

1. Modes of Operation:

   Fully automated, microprocessor controlled, random access, batch and STAT modes

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes __X___ or No _____

3. Specimen Identification:

   Provided in k073604

4. Specimen Sampling and Handling:

   Provided in k073604

5. Calibration:

   Provided in k073604

6. Quality Control:

   Provided in k073604

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.